

## REMARKS

### Status of the Claims

#### *Pending claims*

Claims 1, 14, 15, 29, 33, 35, 40, 42 to 45, 48, 49, 51, 54, 56, 58, 87, 106, 107, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187 to 190, 192, 203 to 208, 215 to 231 are pending.

Claims 42, 51, 54, 56, 58, 106, 107, 111, 113, 116, 138, 143, 174, 175, 177, 182, 184, 187, 190, 208, 215, 216, 219-224 and 229 to 231 were withdrawn.

Accordingly, claims 1, 14, 15, 29, 33, 35, 40, 43 to 45, 48, 49, 87, 188, 189, 192, 203 to 207, 217 to 218, and 225 to 228 are pending and under consideration.

#### *Claims amended the instant amendment*

Claims 1, 29, 33, 188, 192, 215, 216, 220, 224 and 229 have been amended.

#### *Claims canceled, withdrawn or added in the instant amendment*

Claim 225 is withdrawn. Thus, after entry of the instant amendment claims 1, 14, 15, 29, 33, 35, 40, 43 to 45, 48, 49, 87, 188, 189, 192, 203 to 207, 217 to 218 and 226 to 228 will be pending and under consideration.

Applicants respectfully request entry of the amendments set forth in this response.

### Claim Objections and Rejections

#### *Outstanding Objection*

Claim 225 is objected to for depending on a withdrawn claim.

#### *Outstanding Rejections*

Claims 1, 14, 15, 29, 33, 35, 40, 43 to 45, 48, 49, 87, 188, 192, 203 to 207, 217, 218 and 225 to 228, are rejected under 35 U.S.C. § 112, first paragraph, written description requirement. Claims 1, 14, 29, 33, 35, 188 and 192 are rejected under 35 U.S.C. §102(a), as allegedly anticipated by GenBank Accession no. AF401282 (Lesser). Claims 1, 15, 29, 33, 35, 40, 43 to 45, 48, 49, 87, 188, 192 and 225 to 228, are rejected under 35 U.S.C. §102(b), as allegedly anticipated by Lukyanov (WO 01/27150). Claims 1, 15, 29, 35, 40, 43 to 45, 48, 49, 188 and 192 are rejected under 35 U.S.C. §102(b), as allegedly anticipated by Tsien, et al.,

(US6,140,132). Claims 217 and 218, were alleged to be unpatentable under 35 U.S.C. §103(a) over Lukyanov in view of Short, et al. (WO 00/77262).

Applicants respectfully traverse all outstanding objections and rejections of the claims.

#### Allowable Subject Matter

Applicants thank the Examiner for allowing claim 189.

#### Support for the Claim Amendments

The specification sets forth an extensive description of the invention in the amended claims. Support for high stringency hybridization conditions can be found on page 31, column B, lines 7-9, of the published specification.

#### The Group and Sequence Restriction Requirement (RR) – and Election

The Office alleged that the pending claims are directed to nineteen (XIX) separate and distinct inventions under 35 U.S.C. §121, and Applicants were required to elect a single exemplary nucleic acid or polypeptide for examination. In response, Applicants elected Group I, drawn to, inter alia, nucleic acids, probes, amplification primer pairs, etc., with traverse. In response to the sequence RR, Applicants elected the genus based on the exemplary nucleic acid of the invention SEQ ID NO:29. Applicants requested the Office rejoin Groups III, IV, and XI to the elected Group I (nucleic acids, vectors, transformed cells, etc.), and set forth reasons for their traversal.

After the elected product claims have been found to be allowable, all withdrawn process (methods) claims which depend from or otherwise include all of the limitations of the allowed product claims should be rejoined. MPEP §821.04; pg 800-63, 8th Edition, August 2001; In re Ochiai, 37 USPQ2d 1127 (Fed. Cir. 1995); In re Brouwer, 37 USPQ2d 1663 (Fed. Cir. 1995); 1184 OG 86, 3/26/96.

#### Claim Objection

Claim 225 is objected to for depending on a withdrawn claim. The instant amendment addresses this issue.

Advisory Action of August 13, 2007

Applicants thank the Examiner for the helpful comments in her Advisory Action of August 13, 2007. In the AA, the Office noted that although the amendments from Applicants' last response of May 24, 2007, were not entered, the arguments were at least partially considered and deemed to not overcome all of the rejections. However, Applicants note that the AA also states that since Applicants' amendments were not entered, the arguments presented were moot. Applicants respectfully request the Examiner to reconsider the arguments presented in the response to the final OA (filed May 24, 2007, and reproduced herein) in light of the RCE submitted herewith.

Further, Applicants note that in the AA, the Office alleges that the amendments to claims 1 and 33 raise issues that require further search and consideration because they require consideration of identity to the entire sequence recited in SEQ ID NO:29, where the previous claims only required consideration of identity to a portion of SEQ ID NO:29. However, Applicants respectfully aver that the entire sequence recited in SEQ ID NO:29 has already been considered by the Office because the entire sequence recited in SEQ ID NO:29 was allowed in claim 189.

Issues under 35 U.S.C. §112, first paragraphWritten Description

Claims 1, 14, 15, 29, 33, 35, 40, 43 to 45, 48, 49, 87, 188, 192, 203 to 207, 217, 218 and 225 to 228, are rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventors at the time the application was filed had possession of the claimed invention.

The Office alleges that the specification fails to describe a representative number of species of a very broad genus. Further, the Office alleges that the Applicant only teaches nucleic acid sequences with a very high level of identity (greater than 75%) to the instant SEQ ID NO:29, with little or no teaching as to their functional characteristics.

Applicants respectfully disagree and assert that a representative number of species has been provided, along with adequate description of the functional characteristics of these

members of the genus. Applicants thank the Office for noting that the specification discloses SEQ ID NO:29, which encodes a green fluorescent protein, as well as related nucleic acid sequences (for example SEQ ID NO:1-197 (odd SEQ IDs only) sharing a very high level of identity (greater than 75%). It is indeed these nucleic acids that make up a representative number of species in the claimed genus – nucleic acid sequences having at least 75% sequence identity to the nucleic acid sequence of SEQ ID NO:29 and which encode fluorescent proteins. The Examiner alleges that although the claims disclose numerous sequences with identity to SEQ ID NO:29 ranging from 72% (SEQ ID NO:169) to 99.6% (SEQ ID NO:17), the functional properties of the majority of proteins encoded by these different sequences have not been determined. Applicants respectfully disagree and refer the Examiner to Examples 1 and 2, which describe how the fluorescent proteins encoded by SEQ ID NOs:1-26 were discovered – by activity-based expression screening – from environmental samples (see also Table 1, which indicates that SEQ ID NOs:1-26 were isolated from environmental samples). Further, the specification teaches that SEQ ID NOs:27, 29 and 31 are codon-optimized versions of fluorescent proteins of the invention (SEQ ID NOs:7, 17, and 23, respectively) which were made using SEQ ID NO:17 as the template for optimization (see paragraph [0119] on page 15 of the published specification) and therefore, encode fluorescent proteins. The specification also teaches that SEQ ID NOs:33-198 were artificially created using SEQ ID NOs:27, 29 and 31 as parental sequences (see paragraph [0118] on page 15, as well as Figure 15 and Table 1 of the specification) and also encode fluorescent proteins. The specification also provides data for several of these proteins, showing that they do indeed fluoresce, see, for example, Table 2 which provides experimentally derived excitation and emission wavelengths for a number of fluorescent polypeptides encoded by the claimed genus of nucleic acids. Applicants note that the Examiner expressed uncertainty whether the information provided in Table 2 was derived theoretically or experimentally. Applicants respectfully direct the Examiner's attention to Example 3 which details an exemplary procedure for determining the excitation and emission spectra. The spectra shown in Table 2 were determined similarly to that which is described in Example 3, specifically, by measuring excitation and emission wavelengths with a spectrophotometer. One of skill in the art at the time of filing of the instant application would appreciate that measurement of excitation and emission spectra of a fluorescent protein by spectrophotometry is a routine and simple procedure (see paragraph [0428], page 62 of the

specification). As the specification discloses numerous examples of nucleic acids encoding fluorescent proteins, with a high level of sequence identity to each other, and provides ample data showing the shared functional characteristic of emitting fluorescence, Applicants respectfully submit that the rejection under 35 U.S.C. §112, first paragraph, written description, can be withdrawn.

Issues under 35 U.S.C. §102(a)

Claims 1, 14, 29, 33, 35, 188 and 192 are rejected under 35 U.S.C. §102(a), as allegedly anticipated by GenBank Accession no. AF401282 (Lesser).

In regard to claim 1, the Office alleges that Lesser teaches a sequence with 75% identity to SEQ ID NO:29 over a region of 206 contiguous residues. The Office continues that since claim 1 recites the phrase “at least about 700 contiguous residues”, no minimal number of residues are defined and, as such, the teachings of Lesser anticipate claim 1.

In regard to claim 14, the Office alleges that the sequence taught by Lesser encodes a green fluorescent protein.

In regard to claim 29, the Office alleges the sequence taught by Lesser inherently hybridizes under stringent conditions and that Lesser allegedly teaches a nucleic acid encoding a fluorescent protein with at least 75% sequence identity to SEQ ID NO:29 over at least about 700 contiguous residues.

Regarding claims 33 and 35, the Office alleges that Lesser teaches a probe comprising at least 10 consecutive bases and because of the “at least about” language in claim 1, Lesser anticipates said claims.

Regarding claim 188, the Office alleges that Lesser teaches an isolated, synthetic or recombinant nucleic acid comprising a sequence having at least about 75% identity to SEQ ID NO:29 over at least about 700 contiguous residues.

Regarding claim 192, the Office alleges that sequence taught by Lesser, encoding a fluorescent protein, also has a sequence comprising a combination of segments whose overhangs as described in Figure 15 can anneal to each other. The Office also alleges that Lesser teaches a nucleic acid comprising a sequence having at least about 75% identity to SEQ ID NO:29 over at least about 700 contiguous residues.

The legal standard for anticipation under 35 U.S.C. §102 is one of strict identity. To anticipate a claim, a single prior source must contain each and every limitation of the claimed invention. In re Paulson, 30 F.3d 1475, 1478-79, 31 USPQ2d 1671, 1673 (Fed. Cir. 1994)(citing In re Spada, 911 F.2d 705, 708, 15 USPQ2d 1655, 1657 (Fed. Cir. 1990)). "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." Verdegaal Bros. v. Union Oil Co. of California, 814 F.2d 628, 631, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). MPEP §2131; pg 2100-76, 8<sup>th</sup> ed., Rev. 3, August 2005.

The instant amendments address this issue. After entry of the instant amendment, the claimed invention will encompass a genus of nucleic acids having at least 75% sequence identity to SEQ ID NO:29. Accordingly, because Lesser is not a single prior source that contains each and every limitation of the claimed invention, the rejection under section 102(a) under Lesser can be properly withdrawn. Further, the Office alleges in the AA that the amendments to claims 1 and 33 raise issues that require further search and consideration because they require consideration of identity to the entire sequence recited in SEQ ID NO.: 29, where the previous claims only required consideration of identity to a portion of SEQ ID NO.: 29. However, Applicants respectfully aver that the entire sequence recited in SEQ ID NO.: 29 has already been considered by the Office because the entire sequence recited in SEQ ID NO.: 29 was allowed in claim 189.

#### Issues under 35 U.S.C. §102(b)

Claims 1, 15, 29, 33, 35, 40, 43 to 45, 48, 49, 87, 188, 192 and 225 to 228, are rejected under 35 U.S.C. §102(b), as allegedly anticipated by Lukyanov (WO 01/27150).

In regard to claim 1, the Office alleges that Lukyanov teaches an isolated, synthetic or recombinant nucleic acid encoding a fluorescent protein with at least 75% sequence identity to SEQ ID NO:29 over at least about 700 contiguous residues.

In regard to claim 15, which depends from claim 1, the Office alleges that the nucleic acid taught by Lukyanov encodes a cyan fluorescent protein. It appears that the Office left out the remainder of the reason for rejection of this claim. However, Applicant assumes it because

Lukyanov allegedly teaches a nucleic acid encoding a fluorescent protein with at least 75% sequence identity to SEQ ID NO:29 over at least about 700 contiguous residues.

In regard to claim 29, the Office alleges the sequence taught by Lukyanov inherently hybridizes under stringent conditions to SEQ ID NO:29 and that Lukyanov allegedly teaches a nucleic acid encoding a fluorescent protein with at least 75% sequence identity to SEQ ID NO:29 over at least about 700 contiguous residues.

Regarding claims 33 and 35, the Office alleges that Lukyanov teaches a probe comprising at least 10 consecutive bases and because of the “at least about” language in claim 1, Lukyanov anticipates said claims.

Regarding claim 40, the Office alleges that Lukyanov teaches an amplification primer pair, where the primer pair is capable of amplifying a nucleic acid of claim 1 (Lukyanov allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 43, the Office alleges that Lukyanov teaches an expression cassette comprising the nucleic acid of claim 1 (Lukyanov allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 44, the Office alleges that Lukyanov teaches a vector comprising the nucleic acid of claim 1 (Lukyanov allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 45, the Office alleges that Lukyanov teaches that the vector may be a plasmid, phage or cosmid, as well as use of viral vectors, phagemids, fosmids, bacteriophages and artificial chromosomes.

Regarding claims 48 and 49, the Office alleges that Lukyanov teaches a transformed cell comprising a vector where the vector comprises a nucleic acid of claim 1 (Lukyanov allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 87, the Office alleges that Lukyanov teaches an array comprising the immobilized nucleic acid of claim 1 (Lukyanov allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 188, the Office alleges that Lukyanov teaches a nucleic acid comprising a sequence having at least about 75% identity to SEQ ID NO:29 over at least about 700 contiguous residues.

Regarding claim 192, the Office alleges that sequence taught by Lukyanov, encoding a fluorescent protein, also has a sequence comprising a combination of segments whose overhangs as described in Figure 15 can anneal to each other. The Office also alleges that Lukyanov teaches a nucleic acid comprising a sequence having at least about 75% identity to SEQ ID NO:29 over at least about 700 contiguous residues.

Regarding claims 225 and 226, the Office alleges that Lukyanov teaches a recombinant nucleic acid encoding a fluorescent protein codon-optimized for expression in a host comprising the sequence of claim 1 (Lukyanov allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 227, the Office further alleges that Lukyanov further teaches inclusion of a tag or reporter sequence and also the inclusion of epitope tags (Lukyanov allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 228, the Office alleges that Lukyanov teaches labeled probes and that the nucleic acids may be labeled with epitope tags (Lukyanov allegedly anticipates claim 1 because of the “at least about” language).

The instant amendments address this issue. After entry of the instant amendment, the claimed invention will encompass a genus of nucleic acids having at least 75% sequence identity to SEQ ID NO:29. Accordingly, because Lukyanov is not a single prior source that contains each and every limitation of the claimed invention, the rejection under section 102(b) under Lukyanov can be properly withdrawn.

Claims 1, 15, 29, 35, 40, 43 to 45, 48, 49, 188 and 192 are rejected under 35 U.S.C. §102(b), as allegedly anticipated by Tsien, et al., (US6,140,132).

In regard to claim 1, the Office alleges that Tsien teaches an isolated, synthetic or recombinant nucleic acid encoding a fluorescent protein with at least 75% sequence identity to SEQ ID NO:29 over at least about 700 contiguous residues.

In regard to claim 15, which depends from claim 1, the Office alleges that the nucleic acids taught by Tsien encodes a green fluorescent protein and a cyan fluorescent protein, respectively (Tsien allegedly anticipates claim 1 because of the “at least about” language).

In regard to claim 29, the Office alleges the sequence taught by Tsien inherently hybridizes under stringent conditions to SEQ ID NO:29 and that Tsien allegedly teaches a



nucleic acid encoding a fluorescent protein with at least 75% sequence identity to SEQ ID NO:29 over at least about 700 contiguous residues.

Regarding claim 40, the Office alleges that Tsien teaches an amplification primer pair, where the primer pair is capable of amplifying a nucleic acid of claim 1 (Tsien allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 43, the Office alleges that Tsien teaches an expression cassette comprising the nucleic acid of claim 1 (Tsien allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 44, the Office alleges that Tsien teaches a vector comprising the nucleic acid of claim 1 (Tsien allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 45, the Office alleges that Tsien teaches that the vector may be a plasmid, phage, cosmid, viral vectors, phagemids, fosmids, bacteriophages and artificial chromosomes.

Regarding claims 48 and 49, the Office alleges that Tsien teaches a transformed cell comprising a vector where the vector comprises a nucleic acid of claim 1 (Tsien allegedly anticipates claim 1 because of the “at least about” language).

Regarding claim 188, the Office alleges that Tsien teaches a nucleic acid encoding a fluorescent protein and having at least about 75% identity to SEQ ID NO:29 over at least about 700 contiguous residues.

Regarding claim 192, the Office alleges that sequence taught by Tsien, encoding a fluorescent protein, also has a sequence comprising a combination of segments whose overhangs as described in Figure 15 can anneal to each other. The Office also alleges that Tsien teaches a nucleic acid comprising a sequence having at least about 75% identity to SEQ ID NO:29 over at least about 700 contiguous residues.

The instant amendments address this issue. After entry of the instant amendment, the claimed invention will encompass a genus of nucleic acids having at least 75% sequence identity to SEQ ID NO:29. Accordingly, because Tsien is not a single prior source that contains each and every limitation of the claimed invention, the rejection under section 102(b) under Tsien can be properly withdrawn.

Issues under 35 U.S.C. §103(a)

Claims 217 and 218, were alleged to be unpatentable under 35 U.S.C. §103(a) over Lukyanov in view of Short, et al. (WO 00/77262), as describe in detail in section 10, pages 18 to 20, of the Office Action.

The instant amendments address this issue. After entry of the instant amendment, the claimed invention will encompass a genus of nucleic acids having at least 75% sequence identity to SEQ ID NO:29. Accordingly, Lukyanov neither teaches nor suggests this genus of nucleic acids, and Short does not cure this defect in Lukyanov. Accordingly, because the cited art Lukyanov and Short do not teach or suggest the claimed invention, the rejection under section 103(a) can be properly withdrawn.

## CONCLUSION

In view of the foregoing amendments and remarks, Applicants believe that the Examiner can properly withdraw the rejection of the pending claims under 35 U.S.C. §112, first paragraph, written description, 35 U.S.C. §102(a), 35 U.S.C. §102(b) and 35 U.S.C. §103(a). Applicants believe that all claims pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested.

Applicants believe that no additional fees, outside of the two month extension of time fees, are necessitated by the present response and amendment. However, in the event any such additional fees are due, Applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in the connection with the filing of this document to Deposit Account No. **50-0661**, referencing docket no. **D1410-2US**. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account. Please credit any overpayment to the Deposit Account.

Should any questions arise, the Examiner is invited to contact the undersigned at 858-526-5450 or [lynn.linkowski@verenium.com](mailto:lynn.linkowski@verenium.com).

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Respectfully submitted,

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